American Journal of Hematology 62:56–57 (1999)

Splenectomy During Partial Remission in Thrombotic Thrombocytopenic Purpura With Prolonged Plasma Exchange Dependency

Michael J. Mant*, A. Robert Turner, D. Bruce C. Ritchie, and Loree M. Larratt

Department of Medicine, Division of Clinical Hematology, University of Alberta, and University of Alberta Hospital, Edmonton, Alberta, Canada

Some patients with thrombotic thrombocytopenic purpura (TTP) remain plasma-exchange-dependent for prolonged periods of time. This exposes patients to risk, uses substantial resources, and requires prolonged hospitalization. We have splenectomized 7 such patients following 25–42 plasma exchanges while patients were in partial remission only and were clinically stable. In 6 patients, including 1 with TTP secondary to mitomycin C, thrombocytopenia promptly resolved. Relapse has not occurred during 18 or more months of observation. The seventh patient did not respond. We conclude that splenectomy should be considered as an alternative to continued plasma-exchange therapy in such patients. Am. J. Hematol. 62:56–57, 1999. © 1999 Wiley-Liss, Inc.

Key words: thrombotic thrombocytopenic purpura; hemolytic uremic syndrome; thrombotic microangiopathy; splenectomy; mitomycin C

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is characterized by thrombocytopenia and microangiopathic hemolytic anemia [1]. Neurologic and renal abnormalities are common, and fever may occur. With plasma-exchange therapy (PE), the mortality is now <20% [1–4]. Some patients with TTP have exacerbations after initial response to PE and some remain PE-dependent for a prolonged time [2–7]. These features place patients at risk of fatal relapse and treatment complications. Usual recommended treatment has been continued PE [2–4]; alternative therapies have also been advised [5–7].

We report the use of splenectomy in 7 patients with TTP who remained in partial remission only after 25 or more PEs. One patient had TTP secondary to mitomycin C, a disorder with a poorer prognosis [3].

MATERIALS AND METHODS

The seven patients, who presented between December 1995 and 1997 had thrombocytopenia, microangiopathic hemolytic anemia, and an elevated lactate dehydrogenase. Central nervous system abnormalities were present in four patients and an elevated creatinine in three. Prior to splenectomy each patient had PE's of 1–1½ plasma volumes daily, with fresh frozen plasma, until the platelet count exceeded 140×10^9/l for more than 2 days. The fresh frozen plasma was changed to cryosupernate plasma if deterioration occurred or when at least 5 days of fresh frozen plasma therapy had proven incompletely successful. Each patient received corticosteroids, aspirin, and packed red blood cell transfusions. Vincristine therapy in 4 patients and intravenous immunoglobulin therapy in 6 patients had led to no improvement. Status at splenectomy is shown in the table. Splenectomies were uneventful. After splenectomy PE was discontinued when the platelet count exceeded 150×10^9/l. Platelet counts returned to normal at 4, 13, 3, 4, 3, and 3 days after splenectomy in patients 1–6, respectively. Throm-

*Correspondence to: Michael J. Mant, MB. Ch.B., 2E3.32 W.M.C., University of Alberta, Edmonton, Alberta, Canada T6G 2R7.

Received 18 February 1999; Accepted 5 May 1999

TABLE I. Status at Splenectomy and Highest Platelet Count After Splenectomy

	1	2[a]	3	4	5	6[b]	7
Platelet Count ($\times 10^9$/l)	99	76	129	122	73	107	44
No. phereses performed	31	42	41	29	25	27	28
Units of plasma	703	339	478	650	545	535	441
No. of exacerbations[c]	3	0	2	2	1	1	1
Days to splenectomy	32	43	52	29	27	32	29
Highest platelet count ($\times 10^9$/l) within 14 days of splenectomy	375	190	528	256	255	668	103

[a]TTP secondary to mitomycin C.
[b]TTP occurred during pregnancy.
[c]Exacerbations defined as platelets $<100 \times 10^9$/l for 2 days after 2 or more days at $>150 \times 10^9$/l or by a 50% decrease for 2 days after an increase to $>50 \times 10^9$/l for 2 or more days.

bocytopenia has not recurred in these patients during observation periods of 37, 36, 34, 26, 26, and 18 months. The highest platelet counts reached within 14 days of splenectomy are shown in the table. Patient 7 did not recover and died 73 days after splenectomy of complications of TTP.

DISCUSSION

Despite treatment with PE and corticosteroids, death, long-term sequelae [2], a chronic relapsing course [3,4, 8], and a need for prolonged PE treatment in some patients remain problems in TTP [2–4]. Bell [4] has reported that 52% of 319 patients experienced a relapse or exacerbation within 30 days, and some investigators have suggested that PE should continue for 20 to 30 days to prevent relapses [3,4].

Splenectomy has a long history as a treatment for TTP [3]. Crowther et al. [8] have recently reported its successful use in 6 patients in hematologic remission with a chronic relapsing course. Splenectomy has had variable success, but with considerable morbidity and mortality, in patients unresponsive to PE who have often been acutely ill [3–7].

Patients with early deterioration and incomplete response have often been treated with antiplatelet agents, corticosteroids, intravenous IgG, vincristine, and other immunosuppressants. A few such patients have been treated with splenectomy, although usually after brief PE only [2–7]. Views on the need for this, and on its efficacy, differ. Usual treatment for such patients has been to continue PE, sometimes for many months [2–4]. Adoption of this strategy leaves patients at potential risk for a fatal relapse, of the occasional complications of PE, and of potential complications of the large volumes of blood products used. During this time, patients also consume substantial resources.

We have had successful experiences with splenectomy in patients with chronic relapsing disease. We therefore utilized splenectomy for patients with prolonged PE dependency. In 6 of 7 consecutive patients, improvement was almost immediate and each has remained in remission for 18 months or longer. One patient had TTP secondary to mitomycin C, a disorder with a particularly poor prognosis, and without a clearly defined treatment [3].

TTP is a rare disorder with unpredictable behaviour. Nevertheless, it is likely that the responses seen in our patients resulted from splenectomy. Benefit to these patients, including earlier discharge from hospital, was substantial. Although each of our patients might have eventually recovered with continued PE therapy, we suggest that splenectomy should be considered in such patients. Our results indicate that it can be undertaken safely and successfully in relatively stable patients even when a complete remission has not been obtained.

ACKNOWLEDGMENT

The assistance of Pat Donahue, MN, with data extraction and preparation is gratefully acknowledged.

REFERENCES

1. Rock GA, Shumak KH, Buskard NA, Blanchette VS, Kelton JG, Nair RC, Spasoff RA, and the Canadian Apheresis Study Group. Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. Canadian Apheresis Study Group. N Engl J Med 1991;325:393–397.
2. Hayward CP, Sutton DM, Carter WH Jr, Campbell ED, Scott JG, Francombe WH, Shumak KH, Baker MA. Treatment outcomes in patients with adult thrombocytopenic purpura-hemolytic uraemic syndrome. Arch Int Med 1994;154:982–987.
3. George JN, El-Harake M. Thrombocytopenia due to enhanced platelet destruction by nonimmunologic mechanisms. In: Beutler E, Lichtman MA, Coller BS, Kipps TJ, editors. Williams hematology, 5th. ed. New York: McGraw-Hill; 1995. p 1290–1355.
4. Bell WR. Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome relapse: frequency, pathogenesis, and meaning. Sem Hematol 1997;34:134.
5. Onundarson PT, Rowe JM, Heal JM, Francis CW. Response to plasma exchange and splenectomy in thrombotic thrombocytopenic purpura. A 10-year experience at a single institution. Arch Int Med 1992;152: 791–796.
6. Thompson CE, Damon LE, Ries CA, Linker CA. Thrombotic microangiopathies in the 1980s: clinical features, response to treatment, and the impact of the human immunodeficiency virus epidemic. Blood 8:1890–1895, 1992.
7. Winslow GA, Nelson EW. Thrombotic thrombocytopenic purpura; Indications for and results of splenectomy. Am J Surg 1995;170:558–563.
8. Crowther MA, Heddle N, Hayward CPM, Warkentin T, Kelton JG. Splenectomy done during hematologic remission to prevent relapse in patients with thrombotic thrombocytopenic purpura. Ann Int Med 1996;125:294–296.